

REMARKS

I. Amendments to the Claims:

Claims 26, 41, 49, 82-83, and 85 were pending and under examination in the instant application.

Claims 27-34, 36-40, 42-44, 46-48, 50-70, 73-75, 80, 81, and 84 were withdrawn by the Examiner as drawn to a non-elected invention.

By this paper, claims 26 and 83 are amended, and claims 41, 49, and 82 are cancelled, without prejudice. Support for the claim amendments can be found throughout the specification and claims as filed. For example, support for methods for treating or increasing resistance to a viral infection in a mammalian subject can be found at, *inter alia*, page 33, lines 24-26. Also, support for methods of increasing the production of naïve T lymphocytes can be found at, *inter alia*, page 7 lines 29-31, page 27 lines 4-6, page 35 lines 12-14, page 74 lines 6-7, page 95 lines 17-18, and Figure 44. Accordingly, no new matter has been added by these amendments.

Upon entry of the instant amendment to the claims, claims 26, 83, and 85 will be pending and under examination in this application.

II. Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 26, 41, 49, 82-83, and 85 are rejected under 35 U.S.C. § 112, first paragraph, for purportedly failing to comply with the enablement requirement (*see*, Office Action, pages 2-4).

Specifically, the Office Action asserts that “the term ‘patient’ in claim 26...is problematic because, given the broadest possible interpretation, this could include animals such as insects and fish” in which castration might not have the claimed effects on the thymus. In support of this contention, the Office Action cites Deanesly *et al.* (1927, *J. Cell. Sci.*, 281 p113-145), which allegedly teaches that the involution of the thymus in fish is not tied to sexual maturity as it is in mammals. (*See*, Office Action, page 3).

In response Applicant notes that the amended claims, as presented herein, are specifically directed to treating or increasing resistance to viral infection in a mammalian or avian subject.

The Examiner acknowledges that the specification is "enabling for a method of treating or increasing resistance to viral infection in a mammal'" (*see*, Office Action, page 2, emphasis added).

Applicant avers that the application as filed also supports and enables a method of treating or increasing resistance to viral infection in an avian. The specification as filed states that "this invention may be used with any animal species (including humans) having sex steroid driven maturation and an immune system (*see* page 33, lines 24-25 of the application as filed). Applicants submit that, at the time of the invention it was known in the art that avian species have sex steroid driven maturation and an immune system, and furthermore it was known in the art at the time of the invention that the thymus of avian species functions in a similar way to that of mammals. For example, in a paper by Cooper *et al.* (1965, *Journal of Experimental Medicine*, 123, p75-102) a copy of which is submitted concurrently herewith in an Information Disclosure Statement, it was shown that "the thymus and the system of lymphocytes dependent upon it play the same functional role in the chicken as in mammals" (*see* Cooper *et al.*, p 76, second paragraph). Accordingly, Applicants submit that one of skill in the art would have understood the present invention, as described in the application as filed, as encompassing a method of treating or increasing resistance to viral infection in an avian species. Furthermore, Applicants submit that the specification is enabling for methods of treating or increasing resistance to viral infection in animals having sex steroid driven maturation and an immune system, including avians.

In view of the amendments to the claims presented herein, and the foregoing remarks, Applicant submits that rejection of the claims for lack of enablement under 35 U.S.C. §112, first paragraph, has been overcome. Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. § 103(a)

Claims 26, 41, 49, 82-83, and 85 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Windmill *et al.* (1998, *Tissue and Cell.*, 30, p104-111) in view of Musey *et al.* (1997, *N. England. J. Med.*, 337, p1267-1274) and Kendall *et al.* (1990, *Cell Tissue Res.*, 261, p6555-564).

Specifically, the Office Action states that Windmill *et al.* teaches that T cell numbers are increased following castration in rats, but does not teach a method of treating viral infection comprising chemical castration. The Office Action goes on to state that that Musey *et al.* teaches that in HIV-1 infected patients cytotoxic T cell numbers decrease over time, and that Kendall *et al.* teach that chemical castration using Goserelin increases thymic weight in rats. The Office Action then asserts that it would obvious to the ordinary artisan to modify the method taught by Windmill *et al.* to treat immunocompromised patients infected with HIV-1 to increase thymus activity by increasing cytotoxic T lymphocyte output.

By this paper, Applicants have amended the pending claims to recite a method for treating or increasing resistance to a viral infection in a mammalian or avian subject, comprising increasing the production of naïve T lymphocytes in the thymus of the subject by performing chemical castration. The ability to stimulate production of naïve T lymphocytes is functionally important in treating or increasing resistance to a viral infection. Support for methods of increasing the production of naïve T lymphocytes can be found at, *inter alia*, page 7 lines 29-31, page 27 lines 4-6, page 35 lines 12-14, page 74 lines 6-7, page 95 lines 17-18, and Figure 44 of the specification as filed. For example, the description provided at page 27 lines 4-6, which describes the data illustrated in Figure 44, states that following LHRH agonist treatment “there was a selective increase in the proportion of naïve (CD45RA+) CD4+ cells, with the ratio of naïve (CD45RA+) to memory (CD45RO+) [cells] in the CD4+ T cell subset increasing in 6/9 of the human patients.”

None of the cited art, either alone or in combination, teaches or suggests that chemical castration may be used to increase the production of naïve T lymphocytes. Instead the cited art shows only that T cell numbers and/or activity are increased. Both Kendall *et al.* and Windmill *et*

al. examine the total number of T-cells using pan T-cell antibodies in sections of thymus and spleen, which is inadequate to determine the nature of the T-lymphocytes in the periphery. Furthermore the knowledge of one skilled in the art also does not provide the necessary teaching or suggestion that chemical castration may be used to increase the production of naïve T lymphocytes. An expansion of existing cytotoxic T lymphocytes following chemical castration would be of little value in controlling HIV viral replication and slowing the decline of CD4+ cells. It is critical for halting viral replication that naïve T cells are produced.

Because neither Windmill *et al.*, Musey *et al.*, nor Kendall *et al.* teach or suggest that chemical castration can increase the production of naïve T lymphocytes, this combination of references fails to teach all of the elements of the present claims, and accordingly fails to support a *prima facie* case for obviousness.

Furthermore, the cited references provide no expectation of success for the claimed methods. As stated above, the ability to stimulate production of naïve T lymphocytes is functionally important in treating or increasing resistance to a viral infection. A method that results in expansion of existing T-lymphocytes would not be as effective. Accordingly, one of skill in the art, upon reading the cited art, would not know that castration can stimulate production of naïve T-lymphocytes, and thus would have no reason to expect that chemical castration would be useful in treating, or increasing resistance to, a viral infection, such as an HIV infection. It was not until the present inventors found that chemical castration stimulates the production of naïve T lymphocytes, that one would have had any reason to believe that castration might be useful in treating, or increasing resistance to, a viral infection. To conclude otherwise would amount to an impermissible use of hindsight.

In view of the amendments to the claims presented herein, and the foregoing remarks, Applicant submits that the rejection of the claims under 35 U.S.C. §103(a) has been overcome. Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

CONCLUSIONS

In view of the amendments and arguments provided above, Applicant respectfully requests reconsideration and withdrawal of the outstanding rejections.

Applicant petitions for a two-month extension of time to respond to the outstanding Office Action. Other than the fees for the extension of time and the filing of the Supplemental IDS, no additional fees are believed to be due in connection with this paper; however, in the event that any unforeseen fees are due, please charge any such required fee, or credit any overpayment in fees, to Deposit Account No. 08-0219

The Examiner is invited to telephone the undersigned at the telephone number given below if it would advance prosecution of this application.

Respectfully submitted,

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